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New Technologies to Visualize T Cell Function: A Picture Tells a Thousand Words

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INTRODUCTION

If the science of immunology has one shortcoming, it is a tendency to anthropomorphize the behavior of the cells that subserve immune function. The language of immunology abounds with human attributions such as "tolerance," "memory," "killer," "helper," "foreign," "naive," "danger," and most recently "regulator." Although these words serve as the best descriptors of reality we currently have, they are ultimately inadequate, liable to loose interpretation, and sometimes downright misleading. The problem is that our knowledge of the cellular basis of adaptive immunity, at least in humans, is largely compiled from indirect sources such as in vitro experiments performed in artificial and hostile laboratory environments, and interpretation of cellular function is based largely on the use of flow cytometric detection of surface markers or the proliferative or cytotoxic behavior of a bulk population. Although these approaches have served us well for the past 35 yr or so, since the discovery of the T lymphocyte, they do not do justice to the dynamic complexity of the immune response or recapitulate what happens in the intact organism. To fully understand the events inside the lymph node when T cells engage APCs, we need ways to directly visualize T cell/APC interactions in situ. To clearly understand how the cohorts of molecules involved in TCR engagement are orchestrated temporally and geographically, we need to construct a molecular-level picture of the assembly of the macromolecular structure in totality that we call the "immune synapse." To appreciate what happens to the T cell after receptor engagement and activation, we need to track step by step the cascades of molecular interactions that occur within the cytoplasm of the individual activated T cell. In this review 3 investigators describe new technologies that have led to discoveries that greatly extend our knowledge of T cell immunity and lead to a more accurate, less anthropomorphic, view of the day-to day life of the T lymphocyte.